Table 1
Multivariate OS Analysis

	Total Cohort HR 95% CI	*P*	50-59 Years HR 95% CI	*P*	60-73 Years HR 95% CI	*P*
STANDARD VARIABLES						
Age >60	1.83 1.26-2.65	.001				
HCT-CI >=3	1.56 1.07-2.28	.02	1.50 .88-2.53	.13	1.72 .99-2.98	.05
Active Disease	1.31 .90-1.90	.16	1.54 .92-2.58	.10	1.27 .71-2.27	.42
Ablative Regimen	1.54 1.02-2.31	.04	2.14 1.24-3.69	.01	1.07 .54-2.10	.85
GA VARIABLES						
IADL Impairment	2.38 1.59-3.56	<.001	1.86 1.07-3.24	.03	3.25 1.75-6.05	<.001
Slow Walk Speed	1.80 1.14-2.83	.01	1.16 .60-2.28	.66	3.27 1.68-6.39	.001
Reduced Mental Health	1.67 1.13-2.48	.01	1.55 .92-2.62	.10	1.87 1.01-3.49	.04
Low Albumin	1.52 .94-2.46	.09	1.23 .57-2.63	.60	2.62 1.26-5.47	.01
High CRP	2.51 1.54-4.09	<.001	1.89 .94-3.79	.07	3.13 1.52-6.46	.002

*Each GA measure analyzed separately, adjusting for standard variables

in univariate analysis, adjusting for standard HCT variables (age, HCT-CI, conditioning regimen intensity, disease risk).

Results: 203 adults >=50 years completed GA and underwent HCT. Mean age was 59 years (range 50-73); 45% had high disease risk, 76% received reduced intensity conditioning, and 14% underwent cord blood HCT. With median follow-up of 36 months, IADL limitations ($P < 0.0001$), slow walk speed ($P = 0.01$), low SF36-MCS ($P = 0.01$), and high CRP ($P < 0.001$) were significantly associated with inferior OS, independent of standard HCT variables. The prognostic effect of these GA variables was greater in older recipients (Table 1). We then created a simple risk score with 1 point for the most prognostic functional measure (IADL impairment) and 1 point for comorbidity (HCT-CI >=3). This significantly stratified outcomes, particularly in those ≥60 years, such that 2-year OS was 63%, 29%, and 0% for 0, 1, and 2 points, respectively.

Conclusion: GA measures confer independent prognostic utility in older HCT recipients, especially in those >=60 years. Implementation of GA prior to HCT may aid in appropriate selection of older adults for HCT.

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Kinetics of Chimerism and Early Immune Recovery in Patients Receiving Unmodified Peripheral Blood Allogeneic Grafts Followed By Post-HSCT High Dose Cyclophosphamide for Gvhd Prophylaxis

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Background: Recent studies have shown the intravenous administration of high-dose cyclophosphamide (CY) in the early post-transplant period to be a strategy for GvHD prophylaxis in patients with hematologic malignancies who receive allogeneic marrow grafts from alternative donors. We evaluated the outcomes of patients who received HPC-Apheresis products to compare the impact of post-transplant CY on neutrophil engraftment, hematopoietic chimerism, and early immune reconstitution in patients who received post-HSCT CY following haplo-identical (HAP), matched unrelated donor (MUD), and mismatched unrelated donor (mMUD) grafts vs. with conventional matched related donor (MRD) graft recipients.

Methods and Results: We transplanted 44 patients (median age, 49 years; range, 20-72 years) with advanced hematologic malignancies n=8 (HAP); 14 (MRD); 17 (MUD); 5 (mMUD). All patients received conditioning regimens based on busulfan or total body irradiation (TBI). High-dose CY (50 mg/kg/day) was administered on days 3 and 4 following HAP and on day 3 following MUD transplant. Peripheral blood lymphocyte reconstitution and quantitative T-cell and myeloid specific donor chimerism (STR) status was assessed on post-HSCT days 30 and 60. Mean time to ANC 500 was 12.5 days for MRD, mMUD and MUD graft recipients. HAP recipients took slightly longer at 15.2 days but not significantly different from others. Day +30 median CD3/CD15 chimerism was 82.3+12.4/99.8+0.5 for MRD; 86.7+16.0/97.6+2.2 for MUD; 87.6+15.3/99.8+0.4 for mMUD; and 98.8+1.8/99.2+1.2 for HAP. Day +30 HAP CD3 chimerism was significantly improved over MRD ($p<0.001$) but not over MUD or mMUD. CD15 chimerism did not differ between groups. Of 30 patients that received CY, 18(60%) and 27(90%) achieved full (>95%) donor CD3+ and CD15+chimerism by day +30, respectively vs. 1 (7%) and 12 (86%) in 16 patients who underwent MRD transplants. Day +30 total T cell recovery was significantly faster in MRD than CY-treated recipients ($p=0.015$) due principally to more robust CD8+ T cell recovery. CD4 T cell recovery remained incomplete in all groups through day +100. Recovery of γδ T cells did not differ between groups. Regulatory T cells are virtually absent. NK cells recover to normal numbers at day +28 in all groups.

Conclusions: Recipients of HAP, MUD and mMUD grafts who received post-HSCT CY show similar engraftment kinetics as those who receive MRD grafts with standard immunosuppression. T-cell engraftment appears to follow myeloid engraftment in those who received post-transplant CY and is generally earlier by day 30 than in MSD graft recipients, although CD3+CD8+ recovery is greater in MRD recipients than others. Taken together, HPC-Apheresis is a reasonable alternative donor graft source when accompanied by post-HSCT CY-based GvHD prophylaxis.

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Haploidentical Transplantation for Advanced Hematologic Malignancies Using Melphalan-Based Conditioning – Mature Results from a Single Center

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Background: Haploidentical stem cell transplantation (HaploSCT) using post-transplant cyclophosphamide (PTCY) has been performed primarily with non-myeloablative conditioning. We are exploring a melphalan-based, myeloablative yet reduced-intensity conditioning (RIC), in an ongoing phase II clinical trial.

Methods: Outcomes of the first 84 pts treated after 01/2009 are reported. 47(56%) pts were males. 74 (88%) pts had their first transplant, 10 (12%) as second transplant. The median age was 46 years (range 19-67). 57 (67.9%) pts were protocol

Table 1

Outcomes overall	All patients (N=84) (%)	Myeloid in CR (N=27) (%)	ALL (N=10) (%)	Lymphoma/ CLL (N=14) (%)	P
NRM	25.7	8.9	33.3	25.0	0.17
Relapse Rate	32.0	24.3	25.0	21.4	0.96
PFS	42.3	66.8	41.7	53.6	0.22
aGVHD II-IV	32.6	26.9	50.0	35.7	0.46
aGVHD III-IV	7.8	0	37.5	7.1	0.0038
cGVHD Lim.+Ext.	21.3	21.7	57.1	17.9	0.11
cGVHD Ext. only	10.2	17.7	17.1	0	0.36

eligible. The conditioning regimen was melphalan 100-140mg/m2 with fludarabine, +/- thiotepa previously described by us (Ciurea SO, BBMT 2012;18:1835). All had a bone marrow graft except 4 pts (95%). Diagnoses were AML/MDS 49 (58.3%), CML 9 (11%), ALL 10 (12%), and lymphoma/CLL 13 (15%) (4 Hodgkin's, 4 NHL, 5 CLL), other 3 (3.6%). 28/46 (61%) pts with myeloid diseases were in CR at transplant, and 15/21 pts with AML in remission had poor-risk cytogenetics. Donors were siblings (N=36), children (N=35), parents (N=12), cousin (N=1).

Results: All pts achieved engraftment except 3 (96.4%), 91.6% with full donor chimerism. Median time to neutrophil engraftment was 18 days (11-43 days). The cumulative incidence of acute and cGVHD for different groups is presented in Table 1. Overall, for the entire cohort, the NRM was 25.7%, relapse rate was 32% and PFS was 42.3%. The median OS for first transplants was 25.6 months (mo) and 6.5 mo for second transplant pts. For pts receiving their first transplant, PFS was similar for those who received full and RIC. Of the 49 pts who had first transplant for AML/MDS, 27 (55.1%) were in complete remission prior to transplant. NRM for these pts was 9%, relapse rate 24.3% and PFS 66.8% at 50 mo of median follow-up (Table 1, Figure 1B).

Conclusions: Melphalan-based conditioning for HaploSCT offers good disease control with low treatment-related mortality. Factors associated with survival were protocol eligibility and remission status for myeloid diseases while the melphalan dose did not impact outcomes. A low relapse rate was observed for lymphoma/CLL pts.

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Related PBSC Donors Age >60 Have High Rates of Baseline and Donation-Related Pain and Slow Recovery: First Report from the Related Donor Safety Study (RDSafe)

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As the use of hematopoietic cell transplantation (HCT) in older patients has increased over the past decade, so too have donations from their older siblings. Prospective data addressing the experiences of older donors are limited, though such donors are more likely than younger donors to have comorbidities, and are often motivated to give in spite of potential risks. To address this lack of data, the NHLBI-funded Related Donor Safety Study (RDSafe) prospectively enrolled related donors of all ages between 2010-2013 at 54 transplant centers in the United States, assessed their pre-donation comorbidities and health status, and followed them for 1 year after donation, collecting detailed information on pain levels and 12 additional frequently noted symptoms, e.g., nausea, vomiting, insomnia. This report describes early experiences of 256 donors age >60.

Results: At baseline there were high rates of pre-G-CSF pain and symptoms in older donors, with 28% experiencing grades 1-3 pain and 17% grades 1-3 symptoms (baseline rates from earlier NMDP data for 41-60 year olds were 9% and 5%, respectively, with no grade 3 or greater). Peak rates of all grades of pain and symptoms at day 5 of G-CSF (day 1 of collection) were 69% and 49%, respectively (see figure). Of note, 11% experienced grades 3-4 pain; in contrast, for 41-60 year old NMDP donors, 89% experienced any grade pain; 3%, grade 3-4 pain. Assessment at 1 month showed that 68% and 78% of older donors had returned to baseline pain and other symptom levels while 16% and 6% still reported grade 2-3 pain and symptoms, respectively (NMDP recovery: 96% at 1 month for both). Univariate analysis of the effect of gender, race, age, and baseline rates of pain and symptoms on G-CSF-related pain and symptoms, and return to baseline at one month was performed. Donors with grade 2-3 pain at

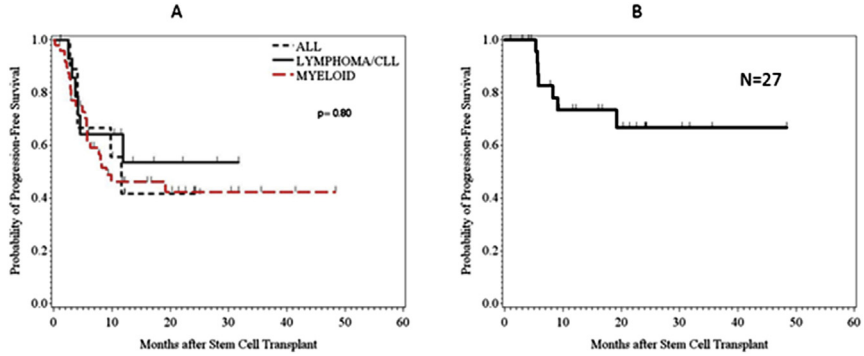

Figure 1. A. PFS first transplants, all patients; B. PFS for myeloid patients in remission.